

less for 3 hours. At the end of the drying period fill the vacuum oven with air dried by passing it through a drying agent such as sulfuric acid or silica gel. Replace the stopper and place the weighing bottle in a desiccator over a desiccating agent such as phosphorous pentoxide or silica gel, allow to cool to room temperature, and reweigh. Calculate the percent loss.

(4) *pH*. Proceed as directed in § 440.80a(b)(5)(ii) of this chapter, using a solution containing 33 milligrams per milliliter.

§ 436.542 Acid resistance/dissolution test for enteric-coated erythromycin pellets.

(a) *Equipment*. Use Apparatus 1 as described in the United States Pharmacopeia XX dissolution test.

(b) *Immersion fluids*. All immersion fluids may be degassed by heating immediately prior to use.

(1) *Acid resistance medium*. Use 0.06*N* hydrochloric acid, pH 1.2.

(2) *Dissolution medium*. Dissolve 6.8 grams of monobasic potassium phosphate in 250 milliliters of water. Add 109 milliliters of 0.2*N* sodium hydroxide and 400 milliliters of water and adjust the resulting solution with 0.2*N* sodium hydroxide to a pH of 6.8±0.1. Dilute to 1 liter.

(c) *Procedure*. Warm the immersion fluids to a temperature of 37° ±5.0° C. Place the contents of one capsule into the basket. Lower the basket into 900 milliliters of acid resistance medium contained in the beaker. Ensure that all air is displaced from the immersed basket and that the pellets remain in the basket. Rotate the basket at the speed of 50 revolutions per minute for an accurately timed period of 1 hour. Remove the basket from the fluid and immediately lower the basket into 900 milliliters of dissolution medium contained in the beaker. Again ensure that all air is displaced from the immersed basket and that the pellets remain in the basket. Rotate the basket at 50 revolutions per minute for an accurately timed dissolution period of 45 minutes. Withdraw a 25-milliliter sample of the dissolution medium from a point midway between the stirring shaft and the wall of the vessel and approximately midway in depth. Filter the sample

through a Whatman 541 filter paper or equivalent, discarding the first 2 milliliters. Assay for erythromycin using the filtrate as the test solution as directed in § 436.105. Repeat the test on five additional capsules.

(d) *Evaluation*. Use the interpretation described in the United States Pharmacopeia XX dissolution test.

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§ 436.543 Acid resistance test for pellet-filled doxycycline hyclate capsules.

(a) *Equipment*. Use Apparatus 1 as described in the United States Pharmacopeia XXI dissolution test.

(b) *Acid resistance medium*. Use 0.06*N* hydrochloric acid, pH 1.2. May be degassed by heating immediately prior to use.

(c) *Procedure*. Warm the acid resistance medium to a temperature of 37±2.0 ° C. Place the contents of one pellet-filled capsule into the basket. Lower the basket into a beaker containing 900 milliliters of acid resistance medium. Ensure that all air is displaced from the immersed basket and that the contents of the pellet-filled capsule remain in the basket.

Rotate the basket at the speed of 50 revolutions per minute for an accurately timed period of 20 minutes. Withdraw a 5-milliliter sample of the acid resistance medium from a point midway between the stirring shaft and the wall of the vessel and approximately midway in depth (this is the sample solution). Assay the sample solution for doxycycline as described in paragraph (d) of this section. Repeat the test on five additional pellet-filled capsules.

(d) *Doxycycline content*—(1) *Preparation of working standard solution*. Dissolve an accurately weighed portion of doxycycline hyclate working standard with 0.1*M* hydrochloric acid to obtain a concentration of 0.01 milligram per milliliter.

(2) *Preparation of sample solution*. Dilute the 5-milliliter sample portion to 25 milliliters with 0.1*M* hydrochloric acid.